REMARKS

The Examiner states that the disclosure is objected to because on page 51 of the specification, the information concerning the ATCC deposit numbers and date of deposit for the cited clones is incomplete and the location of the ATCC should be amended to recite the new Manassas, Virginia address. Applicant has inserted the ATCC deposit numbers and dates as well as the new ATCC address.

Claims 9-20 and 24 are rejected under 35 U.S.C. § 112, first paragraph. The Examiner states that the claims are drawn to polynucleotides derived from a BS203 nucleic acid molecule, wherein said polynucleotide has at least 50% identity with SEQ ID NOS: 1-14 and fragments thereof and that the claims further include nucleic acids which specifically hybridize with "a BS203" nucleic acid sequence and polynucleotides encoding for at least one "BS203 epitope".

Due to the amendments made to the claims, which delete "BS203" language and cancel claim 10 containing hybridization language, it is respectfully requested that the Examiner withdraw this rejection.

Claims 9-20 and 24 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for nucleic acids consisting of the sequence of SEQ ID NOS: 1-14 and sequences fully complementary to SEQ ID NOS: 1-14, it does not reasonably provide enablement for polynucleotides derived from BS203 which share at least 50% identity to SEQ ID NOS: 1-14 or fragments or complements thereof.

Applicant disagrees due to the fact that these sequences are members of the RING finger family. Recently a new class of zinc-finger proteins was identified and designated as the RING finger family. The proteins in this family are characterized by the RING finger motif which is $C\text{-}X_2\text{-}C\text{-}X_{(9\text{-}39)}\text{-}C\text{-}X_{(1\text{-}3)}\text{-}H\text{-}X_{(2\text{-}3)}\text{-}C\text{-}X_2\text{-}C\text{-}X_{(4\text{-}48)}\text{-}C\text{-}X_2\text{-}C$, where X is any amino acid (Borden, K. L. B. and Freemont, P. S., "The RING finger domain: a recent example of a sequence-structure family", *Current Opinion in Structural Biology,* **6**:395-401, 1996 and Saurin, A. J., et al., "Does this have a familiar RING?", *TIBS* **21**:208-214, (1996)). The RING finger motif is cysteine-rich and the cysteine and histidine residues function together as a unique zinc ligation system referred to as the "cross-brace' motif. Two zinc atoms are bound by this domain. BS203 (SEQ ID NO:17) contains a region that closely agrees with the RING finger motif starting at the 9th amino acid residue from the N-terminal end to the 48th amino acid residue. The RING finger motif in BS203 is the following:

CICLHVFVEPVQLPCKHNFCRGCIGEAWAKDSGLVRCPEC. The cysteine and histidine residues are underlined which match the RING finger motif above. The only difference is that the motif has two amino acid residues between the first two cysteine residues while the BS203 RING finger domain has one residue between the first two cysteines.

The RING finger family is comprised of a variety of proteins including proteins with oncogenic potential. These include the breast cancer susceptibility gene BRCA1, the RET finger protein (Rfp), the transcriptional intermediary factor (TIF1), the Cbl and Bmi-1 proto-oncoproteins and Mel18, a nuclear DNA-binding protein isolated from melanomas (Saurin, A. J., et al., "Does this have a familiar RING?", *TIBS*, **21**:208-214, (1996)). The PML protein is a fusion protein found in patients with acute promyelocytic leukemia (Saurin, A. J., et al., "Does this have a familiar RING?", *TIBS*, **21**:208-214, (1996)). The TRAF protein family are RING finger proteins that function in signal transduction pathways and CART1 is one that is associated with breast carcinomas and metastasis (Regnier, C.H. et al., *J. Biol. Chem.*, **270**:25715-21, (1995)). In addition, RING finger proteins have been identified which bind to steroid receptors and most likely their function is to modulate the receptors' transactivating functions. SNURF contains the RING finger motif, associates with androgen receptor, and enhances androgen receptor dependent transactivation (Moilanen, A.-M., et al., "Identification of a novel RING finger protein as a coregulator in steroid receptor-mediated gene transcription", *Molecular and Cellular Biology*, **18**:5128-5139, (1998)). Another RING finger protein is the estrogen-responsive finger protein (efp). Efp expression is regulated by estrogen and it may function as a transcription factor by amplifying the action of estrogen in gene regulation (Inoue, S. I., et al., "Genomic binding-site cloning reveals an estrogen-responsive gene that encodes at RING finger protein", *Proc. Natl. Acad. Sci.*, **90**:11117-111121, (1993)).

There is a subfamily of RING finger proteins called the tripartite subgroup which is characterized by three domains, the RING finger, the B box, and a coiled-coil domain (Saurin, A. J., et al., "Does this have a familiar RING?", *TIBS*, **21**:208-214, (1996)). BS203 is a new member of the tripartite subgroup. The general sequence of the B box motif is C-X_2-H-X_7-C-X_7-C-X_2-C-X_5-H-X_2-H and it occurs downstream of the RING finger domain (Reddy, B. A., et al., "A novel zinc finger coiled-coil domain in a family of nuclear proteins", *TIBS*, **17**:344-45, (1992)). BS203 contains a B box downstream from

its RING finger sequence beginning at the 138th amino acid residue and ending at the 170th residue. The B box sequence in BS203 is the following: CPQHNAYRLYHCEAEQVAVCQYCCYYSGAHQGH. The cysteine and histidine residues are underlined which match the B box motif above. B box domains are immediately followed by a coiled-coil domain (Reddy, B. A., et al., A novel zinc finger coiled-coil domain in a family of nuclear proteins. TIBS 17: 344-45, 1992) which is also observed for BS203. A program available on the Internet was used to analyze the BS203 sequence for a coiled-coil domain (http://www.ch.embnet.org/software/COILS_form.html). One is present immediately C-terminal to the B box domain as predicted beginning at about amino acid residue 170 and continuing to residue 250 and possibly to residue 290 of BS203 (exhibit A). Proteins in the tripartite subgroup found to be cancer-associated are PML, Rfp, and TIF1 (Saurin, A. J., et al., "Does this have a familiar RING?", *TIBS*, **21**:208-214, (1996)).

Thus, based on the above identifying characteristics of the claimed sequences and the amendments to the claims raising the percent identity, one skilled in the art is fully enabled to identify claimed sequences and it is respectfully requested that this rejection be withdrawn.

The Examiner further states that claims 15 and 24 are directed to polynucleotides which comprise a sequence encoding at least one BS203 epitope, but the specification does not identify and BS203 epitopes and no guidance is provided as to how one of skill in the art would select appropriate fragments of a BS203 protein which function as an epitope.

The methods for identifying epitopes in a novel peptide sequence are well known and described in both the scientific, commercial, and patent literature. For example, M. H. Van Regenmortel describes how to predict epitopes from the primary sequence of a protein. (See "Protein structure and antigenicity", *Int J Rad Appl Instrum B.*, **14(4)**:277-80, 1987.)

Further, Perkin-Elmer Biosystems, a major provider of DNA sequencing and peptide synthesizing instruments has established a public website which describes how to select peptides which reflect the epitopes of a protein. (See http://www.pebio.com/pa/340913/html/chapt2.html#Choosing the Epitope.) This electronic publication was posted in 1996 and basically describes the process employed by the inventors of the current patent application.

In addition, patent application PCT/US97/00485 describes in detail how to identify epitopes from peptide sequences. The sequence can be scanned for hydrophobicity and hydrophilicity values by the method of Hopp, Prog. Clin. Biol. Res. 172B: 367-377 (1985) or the method of Cease et al, J. Exp. Med. 164: 1779-1784 (1986) or the method of Spouge et al, J. Immunol. 138: 204-212 (1987). Commercial software programs to implement these methods are available.

Claims 9-20 and 24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite and vague over the recitation of "BS203". This rejection is deemed moot since Applicant has deleted this language.

Claims 9-20 and 24 are also rejected by the Examiner as indefinite over the recitation of "derived" alleging this term is not clearly defined in the specification. This language is defined on page 11 starting on line 16. However, in an effort to expedite prosecution, Applicant has deleted this language and obviated this rejection.

Claims 9-15, 17-20 and 24 are rejected under 35 U.S.C. § 102(b) as being anticipated by Inoue (Proceedings of the National Academy of Sciences (December 1993) 90: 11117-11121). Inoue (Figure 2) teaches polynucleotides encoding the estrogen-responsive finger (efp) gene wherein the efp polynucleotides share at least 50% identity with a fragment of SEQ ID NO: 14. Due to the amendments to the claims, which deleted "fragment" language from the claims, this rejection is deemed moot.

The Examiner continues stating that with respect to claims 10 and 11, because of the open claim language "has", the claims are inclusive of polynucleotides which contain within them 20-50 or 15-20 nucleotides and that the efp polynucleotide comprises 20-50 or 15-20 nucleotides. Because Applicant has canceled these claims, this rejection is deemed moot.

Claims 9-15, 17-20 are rejected under 35 U.S.C. § 102(b) as being anticipated by Hillier, *et al.*, (GenBank Accession No. R77167, N45368 or H15926). The Examiner states that Hillier (GenBank Accession No. N45368) teaches polynucleotides encoding the estrogen-responsive finger (efp) gene wherein the efp polynucleotides share at least 50% identity with a fragment of SEQ ID NO: 14. Again, since the Applicant has deleted "fragement" language, this rejection is deemed moot.

Claim 16 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Inoue in view of Linskens, *et al.* (U.S. Patent No. 5,744,300), the Examiner stating that Inoue (Figure 2) teaches polynucleotides encoding the estrogen-responsive finger (efp) gene

wehrein the efp polynucleotides share at least 50% identity with a fragment of SEQ ID NO: 14 and that Linskens (col. 15-16) teaches that probes comprising EST sequences may be immobilized onto a solid support in order to facilitate hybridization methods and to allow for the detection of cells expressing nucleic acids complementary to said probes. Due to Applicant's amendments, which delete "fragment" language, this rejection is deemed moot.

Claim 16 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Hillier, *et al.*, (GenBank Accession No. R77167, N45368 or H15926) in view of Linksens, the Examiner stating that Hillier (GenBank Accession No. N45368) teaches polynucleotides encoding the estrogen-responsive finger (efp) gene wherein the efp polynucleotides share at least 50% identity with a fragment of SEQ ID NO: 14. Due to Applicant's amendments, which delete "fragment" language, this rejection is deemed moot.

CONCLUSION

In view of the aforementioned amendments and remarks, the aforementioned application is in condition for allowance and Applicant requests that the Examiner withdraw all outstanding objections and rejections and to pass this application to allowance.

Respectfully submitted,

P. A. Billing-Medel, *et al.*

Abbott Laboratories
D377/AP6D-2
100 Abbott Park Road
Abbott Park, IL 60064-6050
(847) 935-7550
Fax: (847) 938-2623

Mimi C. Goller
Registration No. 39,046
Attorney for Applicants